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RECORD OF ORAL HEARING

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte VERNON C. MAINO and MARIA SUNI

Appeal 2007-4487
Application 08/803,702
Technology Center 1600

Oral Hearing Held: April 9, 2008

Before DEMETRA J. MILLS, ERIC GRIMES, and JEFFREY N. FREDMAN, *Administrative Patent Judges*.

ON BEHALF OF THE APPELLANTS:

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The above-entitled matter came on for hearing on Wednesday, April 9, 2008, commencing at 9:03 a.m., at the U.S. Patent and Trademark Office, 600 Dulany Street, Alexandria, Virginia, before Paula Lowery, Notary Registration No. 162073, Notary Public.

THE CLERK: Good morning. This is Appeal Number 2007-4487, Mr. Gerald [sic] Petry.

JUDGE MILLS: Good morning. We're familiar with the issues in your case. You can begin, and you have 20 minutes.

DR. PETRY: What I'd like to do is take the opportunity to focus on a few of the key points in the rejection where we believe the examiner erred, but before I do that, I wanted to say a few things about the actual steps in the biology behind some of the steps and where that figures into the claim.

This is in the field of immunology and the methods are to detect T lymphocytes. These are cells of the immune system and they are part of the class of cells called peripheral blagmononucleocytes (phonetic). They aren't the only ones, but they're in that class.

The claimed method really is a method -- you are culturing these cells with this antigen. The T lymphocytes respond to a very specific antigen, and if the antigen is present, the T lymphocytes become activated. They become stimulated. They become activated and make intracellular cytokines.

So the first part of the method is a cell culture process, and the second part is to detect the synthesis of these intracellular cytokines.

Now, a key feature here in the biology of this is the culturing step is done with a sample containing peripheral blood mononucleocytes, and the stimulation of the T cell isn't just the T cell being exposed to the antigen. It's being exposed to the antigen in this milieu of cells.

There are other cells also in this class called antigen-presenting cells which actually bind to the antigen presented to the T cell on the

surface. These cells also present other molecules called costimulatory molecules on the surface. This is part of the biology of this process.

So what the T cell recognizes is the antigen presented but also in the environment presented on the antigen-presenting cell along with the costimulatory molecule.

Let me jump to the first rejection. The first rejection is a rejection on written description. I think this rejection is a little bit unusual because certainly the specification describes the invention and exactly the breadth which is claimed.

The inventor did describe, did conceive of the invention as using an inhibitor of cytokine secretion. The examiner has given his rejection on the basis that there might be a large number of cytokine secretion inhibitors which weren't described in the specification.

Where we think the examiner erred in this case is the examiner applied an incorrect standard. This particular step of including an inhibitor of cytokine secretion purely for the point of increasing the concentration of newly synthesized cytokines in the cell by stopping them from getting out of the cell, that was known in the art.

That had been described in a number of references. We actually pointed out five references that had been cited in the prosecution history, and all five of those used an inhibitor of cytokine secretion for exactly that purpose.

They're not describing the whole invention, of course, but what they're doing is they're enhancing the detection of cytokines by stopping them from getting out of the cell, increasing the concentration.

So we believe -- and the inventor believes -- that this was just a

known step. He had described it before others in the field had described it before, and there's no need in a patent specification to describe in detail what was already a step known in the art.

JUDGE GRIMES: So if I could paraphrase, your position is that to show possession of this claimed method, it's not necessary to show possession of a whole slew of the cytokine secretion inhibitors because that part of the invention was already known in the art, and those skilled in the art would recognize that you are in possession of the method based on the known compounds that carried out that function?

DR. PETRY: Yes. So this method is a combination method. It's a combination of steps. Some of them are old, some of them are new.

Let me just point out, for example, the next step in the method, the idea of permeabilizing the cells in order to detect the intracellular cytokines, you have to bind them to antibodies. The antibodies have to get inside the cell.

This, too, is a known technique in immunology. The specification describes using this technique and gives a preferred best mode example.

Again, we don't believe that and the examiner didn't think that we needed to describe the whole universe of hypotheticals which may permeabilize the cells. We believe this is the same.

Now, we had also cited another case. We think this is really along the same lines. This is a combination claim. It's a claim that involves multiple steps. It's the known use of an old compound.

It really does go back, I believe, to the same principle. This was known in the art. The inventor just said, basically, use the step which

he had already described previously.

JUDGE FREDMAN: Well, the question I would have is actually not so much from a description standpoint but from an enablement standpoint, because I think I agree with you on the description standpoint.

You have essentially a phosphinase-known inhibitor that you disclose in the spec. The prior art you pointed to also mentioned Monensin. There are other known, one Nocodozole, but the O'Neill reference -- it's pretty clear you get significantly different results based on different inhibitors of cytokine secretion.

Obviously, that's a very broad phrase and things that are lethal to the cell are also going to inhibit cytokine secretion, you know, as the examiner points out.

The question I would ask is, do you think -- what's the argument on the undue experimentation analysis here where you can do -- we know there's a generic out there for stopping cytokines in large quantities, right? Because we're looking for a nominal antigen, so the expression of non-cytokines may not be as high in the ABC context, right?

Your declaration seems to point to that expression may be lower. You have two declarations, one of which points out that it's, like, a hundred lower than some other assets.

DR. PETRY: You've actually brought up a couple of issues, so let me try to address them. The breadth of possible cytokine secretion inhibitors -- first of all, the case I cited, In Re: Feutterer, 319 F.2d 259 (CCPA 1963) really said that all you're doing is citing a known element that's out there in a combination method. You really don't have to explore the full method for enablement.

One can use a cytokine secretion inhibitor --

JUDGE FREDMAN: I think that's probably true when it's predictable. I think in this case when it's an unpredictable element, I don't think that's probably the case law.

The question is, is it predictable that compounds that inhibit cytokine secretion will also not have an impact on cytokine expression?

DR. PETRY: The examiner did speculate on compounds even as you said the toxins, for example. I think one has to think about this in view of what one of skill in the art would know.

This is an assay where you're culturing live cells, and you're trying to look at a cytokine response in live cells. If one introduced a toxin, you're killing it.

JUDGE FREDMAN: There's also a requirement that the cells remain alive. I don't see that in the claim. They all start off alive, obviously, but --

DR. PETRY: The cells start out alive, and actually in steps downstream they're probably killed, but for the initial culturing step, the process of that step, as is taught to one of skill in the art, is to have the cell do a response, which is a live response.

So that would immediately -- one of skill in the art would not use a toxin, which would kill the cell right off.

I actually think this is not particularly distinguished from In Re: Feutterer, which we cited in this case, where, again, the examiner had rejected the claims because of speculation of a broad number of compounds, some of them which might not be functional in the claim.

But in this case, someone clearly knows -- in the art, someone

knows what to go to, and it is a step that's described.

Actually, much in the same way when one draws a claim and says, you know, for example, permeabilizing a cell. There may be compounds that permeabilize a cell that would not be compatible with the reaction.

I don't think that's particularly relevant because the scope of what does work well for this type of reaction, for that method, for that result -- so it's a compound that is known to achieve --

JUDGE FREDMAN: That's the question, right? The number of compounds that would work is kind of the issue. If it's one Brefeldin A, that's different than if essentially all the cytokine inhibitors would work.

DR. PETRY: In this case there are a few that are commonly used in the literature, or described in the literature. There's two of them that are the typical ones, the Brefeldin A and Monensin.

The examiner actually provided post-filing art that showed they don't work exactly the same. However, that art also shows that they both do work. So as far as enablement, I believe they both do work. The fact that two different compounds work a little bit different, that would be within the typical optimization.

In summary, we believe the standard applied in that rejection is improper.

Moving on to the second rejection, which was on enablement. The issue of cytokine secretion also comes up there.

We've had a problem all along trying to understand what's rejected and what's not rejected. We pointed that out in the brief, and we described what we believe is the rejected -- which elements are rejected, or

which elements were cited in the rejection.

The rejection here is based on the assertion that certain critical elements necessary for the claimed invention to work were omitted from the claims.

The examiner cited In Re: Mayhew, 527 F. 2d 1229 (CCPA 1976). We've cited cases where the court has commented on In Re: Mayhew and really restricted where that's applicable. Only in cases where the invention truly would not work if that element were omitted.

Now, as far as actually which elements we're talking about, the examiner has been a little inconsistent. We think we understand this. The examiner in the examiner's reply said it goes back to the 2002 rejection. I believe that's not even consistent internally. There's some elements there which clearly are not at issue.

I'd like to point out that the examiner states in the examiner's reply, "It has always been the examiner's position that only a claim, e.g. claim 66" -- this is a claim that's allowed and not at issue -- "reciting all the minimal steps is enabled."

Claim 66 is claim 19, the broadest claim. We added three elements. One was the use of Brefeldin A, a specific cytokine-secretion inhibitor; the use of slant tubes during the incubation period; and the collection of 50,000 events.

Also in the examiner's reply there are some statements about other steps, and we just think actually these are typos, maybe cut-and-paste-type errors.

For example, the step of culturing the sample with the antigen, this is something we added to the claim back in 2003. The examiner had

acknowledged that in the following two office actions and explicitly removed that rejection. Then all of a sudden, it came back at the very end. We think that doesn't apply.

The examiner also had mentioned added costimulation as a critical element. One of the reasons I pointed out the biology, it's something we also pointed out back in 2003. Costimulation is provided by the antigen-presenting cells. It's already there in the sample.

So the need for costimulation to cite that that's known and it has to be there, well, it is there. What we're talking about in the invention is the use of added costimulation which is a method of enhancing the method.

So turning to the ones that are left to discuss, the ones that distinguished the allowed claim from the claim at issue, claim 19, first is the inhibitor of cytokine secretion. You raised the issue of enablement there.

Again, we feel that the examiner to enable the method should be able to turn to the prior art and say, Use this known method.

There are a small number -- admittedly a small number of compounds which are commonly used in immunology. There are a number of papers which describe both of the ones that are used commonly. There may be others, but that is not -- the fact that there may be others should not prevent the inventor from just relaying what is already known in the art.

So we think that's fully enabled with the breadth of just describing, Use an inhibitor of cytokine secretion.

Now, there were a couple of things brought out from example 4. Example 4 is one of the five examples in the specification. It describes an early experiment. It's described as establishing the assay in the first place. It's sort of a subset of the possible assays here.

The examiner focused on this and on particular language within this one claim. There sort of are two main ones here. The use of slant tubes, which is really just the incubation tube is turned at an angle and spreads out the cells a little bit. That's one of them. The other one is the number of events.

The courts have clarified that In Re: Mayhew is really only applicable where the specification as a whole says that the invention won't work unless you include this.

So things that need to be considered, the specification as a whole, teaching outside that omits the element certainly teaches away from that. The other invention -- anything that describes this is only a preferred example. All of those things are here in this case.

In both of these cases, the invention teaches the invention in broad terms, omitting these elements. The specification also describes in two places, one at the beginning of the specifications and at the end, it emphasizes that the examples are there only as examples, not as describing the full invention.

The other point is these are described not as critical elements that if you left them out, they wouldn't work. They are described as ways of optimizing the invention.

The slant tubes provide maximal response. The number of events collected is related to the accuracy. Accuracy is not a claimed limitation here. It's the accuracy of the invention.

In flow cytometry, flow cytometry looks at one cell at a time and collects data, but when you're all done, still you'll see this by looking at the figures, you get clouds of points. It's still a statistical problem to try to

distinguish the subpopulation that you're interested in -- these antigen-specific T lymphocytes -- from the rest of the cells that are in the sample.

It's well known that if you have a statistical problem, you collect more data, you get a more accurate result. This is guidance for the practical limits of the invention. It's guidance to teach one how to carry out the invention in an accurate way. That sort of guidance is supposed to be provided by the specification, not by the claim itself.

Referring to the number of events, example 3, another one of the examples describes actually carrying out the invention with a 48,000 rather than 50,000. Again, it shows that's not a hard and fast limit.

The examiner rejected or ignored this argument, saying that example 3 didn't have any data. Example 3 is written in the past tense. The first three examples, these are all describing elements of how the invention is carried out.

It describes a two-part invention, but for example, 1 is the culturing step. Examples 2 and 3 refer to the detection part, and it's broken up that way.

It clearly -- the way that's written, it is describing carried-out examples. It's just not providing data. But there's no requirement there that an example that says, We carried this out, that that actually provides the data.

So we think the examiner should have taken that into consideration in viewing the specification as a whole.

JUDGE MILLS: It looks like we're coming up on your time. If you could provide your concluding remarks.

DR. PETRY: On each of these elements we think the examiner

has ignored the things that really need to be considered, ignored the broad language in the specification, omitting the critical feature, which tends to indicate that it's not critical.

The specification clearly describes that these examples are only examples and not the whole invention, nor the teaching of example 3 when that clearly is there. Again, not the full specification.

The examiner treated practical guidance and the practical limits of the invention, which should be provided by the specification. The examiner treated that as a critical element, and we believe that's improper.

The last point is the examiner ignored post-filing evidence just on the basis that he'd already drawn the conclusion that that didn't apply because those elements were described as critical.

But since they're not described as critical, the examiner did admit the post-filing of it, and says it is appropriate. These things do describe the invention more broadly.

I think that wraps up the points I wanted to make. Thank you for your attention.

JUDGE MILLS: Thank you.

(Whereupon, the proceedings at 9:25 a.m. were concluded.)